FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 10:04:35 ON 12 SEP 2003

L1	68729	S	ADENOVIRUS
L2	33610	S	CAPSID
L3	1229238	S	CAPSID OR SURFACE
L4	1618251	S	NON-NATIVE OR LIGAND OR ANTIGEN
L5	255601	S	L4 AND L3
L6	1647	S	L1 AND L5
L7	11	S	NON(W)NATIVE LIGAND
L8	0	S	L7 AND L1
L9	350229	S	LIGAND
L10	362	S	L1 AND L3 AND L9
L11	183		DUP REM L10 (179 DUPLICATES REMOVED)
L12	967236	S	REPLAC? OR RECOMBINANT
L13	4530	S	L1 AND L3
L14	1293	S	L12 AND L13
L15	142	S	L9 AND L14
L16	74		DUP REM L15 (68 DUPLICATES REMOVED)
L17	1305534	S	ANTIGEN
L18	1366	S	L13 AND L17
L19	217479	S	ANTIGEN? AND SURFACE
L20	1053	S	L1 AND L19
L21	33610	S	CAPSID
L22	52	S	L20 AND L21
L23	40		DUP REM L22 (12 DUPLICATES REMOVED)

L16 ANSWER 50 OF 74 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
ACCESSION NUMBER: 2001089480 EMBASE
TITLE: Targetable gene delivery vectors.
AUTHOR: Hallenbeck P.L.; Stevenson S.C.
SOURCE: Advances in Experimental Medicine and Biology, (2000) 465/-(37-46).
Refs: 49
ISSN: 0065-2598 CODEN: AEMBAP
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
016 Cancer
022 Human Genetics
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Adenoviral vectors, which have targeting **ligands** for tumor cells on the **capsid**, no natural tropism, and carry a therapeutic payload should be constructed soon and tested in pre-clinical models. Nevertheless, there are still important considerations for the design and therapeutic use of targetable vectors. Perhaps the single greatest challenge in the future, as it was in the past, will be finding **ligands** that have a higher apparent affinity for tumor and/or tumor endothelial cells then normal cells. However, the advent of many rapidly advancing technologies and information including the sequencing of the human genome, in vivo and in vitro phage display, rapid analysis of gene and protein expression in any context, and new cellular targets such as angiogenic endothelial cells, may provide many opportunities for the discovery of novel and useful **ligands**. In addition, the interests in targeting vectors are rapidly growing with new journals and meetings solely devoted to this subject increasing annually. Within the next 5 years, we should have meaningful clinical data on targetable vectors to reassess our progress.

DOCUMENT NUMBER: 99362675 PubMed ID: 10430860
TITLE: Redirected infection of directly biotinylated **recombinant adenovirus** vectors through cell **surface** receptors and antigens.
AUTHOR: Smith J S; Keller J R; Lohrey N C; McCauslin C S; Ortiz M; Cowan K; Spence S E
CORPORATE SOURCE: Laboratories of Molecular Immunoregulation, National Cancer Institute-Frederick Cancer Research and Development Center, Frederick, MD 21702, USA.
CONTRACT NUMBER: NO1-CO-56000 (NCI)
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1999 Aug 3) 96 (16) 8855-60. Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199909
ENTRY DATE: Entered STN: 19990925
Last Updated on STN: 20000303
Entered Medline: 19990909

AB The inability of **adenovirus** to infect primitive hematopoietic cells presents an obstacle to the use of **adenovirus** vectors for gene transfer to these cell types. Therefore, expanding the tropism of **adenovirus** vectors to unique cell **surface** antigens would be an important development for gene therapy protocols. In this study, we sought to redirect infection of **adenovirus** vectors to primitive human hematopoietic cells that universally express the c-Kit receptor on their cell **surface**. To accomplish this, a vector was constructed by covalently linking biotin molecules to **recombinant adenovirus**, followed by addition of the biotinylated **ligand** for the c-Kit receptor, stem cell factor (SCF), through an avidin bridge. Gene transfer was directed specifically to c-Kit-positive hematopoietic cell lines, resulting in up to a 2,440-fold increase in luciferase expression with frequencies equivalent to **recombinant** virus infection of permissive cells. Substitution of biotinylated antibodies directed against c-Kit, CD34 (binds L-selectin), and CD44 (hyaluronate receptor) receptors for biotinylated SCF resulted in 50-, 8-, and 260-fold increases in reporter gene expression, respectively, demonstrating that infection also could be redirected through antibody-antigen interactions and through antigens other than growth factor receptors. The versatility of this vector was demonstrated further by infection of primary T cells with vectors targeted with antibodies to CD44 (resting and activated T cells) and biotinylated IL-2 (activated T cells only). Taken together, directly biotinylated **adenovirus** vectors represent a versatile and efficient method for redirection of virus infection to specific cells.

L16 ANSWER 63 OF 74 MEDLINE on STN DUPLICATE 31
ACCESSION NUMBER: 1998298563 MEDLINE
DOCUMENT NUMBER: 98298563 PubMed ID: 9634824
TITLE: Targeted gene delivery by tropism-modified adenoviral vectors.
AUTHOR: Douglas J T; Rogers B E; Rosenfeld M E; Michael S I; Feng M; Curiel D T
CORPORATE SOURCE: Gene Therapy Program, University of Alabama at Birmingham 35294, USA.
CONTRACT NUMBER: R01 5025505
SOURCE: NATURE BIOTECHNOLOGY, (1996 Nov) 14 (11) 1574-8. Journal code: 9604648. ISSN: 1087-0156.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199808
ENTRY DATE: Entered STN: 19980828
Last Updated on STN: 19980828
Entered Medline: 19980814

AB The utility of adenoviral vectors for gene therapy is currently limited due, in part, to the widespread distribution of the cellular receptor for the **adenovirus** fiber that precludes the targeting of specific cell types. In order to develop a targeted **adenovirus**, it is therefore necessary both to ablate endogenous viral tropism and to introduce novel tropism. We hypothesized that these two goals could be achieved by employing a neutralizing anti-fiber antibody, or antibody fragment, chemically conjugated to a cell-specific **ligand**. To test this concept, we chose to target the folate receptor, which is overexpressed on the **surface** of a variety of malignant cells. Therefore, we conjugated folate to the neutralizing Fab fragment of an anti-fiber monoclonal antibody. This Fab-folate conjugate was complexed with an adenoviral vector carrying the luciferase reporter gene and was shown to redirect adenoviral infection of target cells via the folate receptor at a high efficiency. Furthermore, when complexed with an adenoviral vector carrying the gene for herpes simplex virus thymidine kinase, the Fab-folate conjugate mediated the specific killing of cells that overexpress the folate receptor. This work thus represents the first demonstration of the retargeting of a **recombinant** adenoviral vector via a non-adenoviral cellular receptor.

L23 ANSWER 16 OF 40 MEDLINE on STN
ACCESSION NUMBER: 1999422052 MEDLINE
DOCUMENT NUMBER: 99422052 PubMed ID: 10490760
TITLE: Coxsackie and **adenovirus** receptor (CAR)-dependent and major histocompatibility complex (MHC) class I-independent uptake of recombinant **adenoviruses** into human tumour cells.
COMMENT: Comment in: Gene Ther. 1999 Sep;6(9):1497-8
AUTHOR: McDonald D; Stockwin L; Matzow T; Blair Zajdel M E; Blair G E
CORPORATE SOURCE: School of Biochemistry and Molecular Biology, University of Leeds, Leeds LS2 9JT, UK.
SOURCE: GENE THERAPY, (1999 Sep) 6 (9) 1512-9.
Journal code: 9421525. ISSN: 0969-7128.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200004
ENTRY DATE: Entered STN: 20000413
Last Updated on STN: 20021217
Entered Medline: 20000403

AB The role of two receptors, previously proposed to mediate the entry of **adenoviruses** into human cells, the coxsackie and **adenovirus** receptor (CAR) and the major histocompatibility complex (MHC) class I heavy chain has been investigated. The expression of MHC class I in many tumours is reduced or absent, therefore if this were a means by which **adenoviruses** gained entry into cells, it would have important implications for their application in cancer treatment. In order to determine if MHC class I heavy chain is involved in **adenovirus** type 5 (Ad5) uptake, the binding of recombinant Ad5 fibre knob domain (which mediates viral attachment) to human cell lines that had greatly different levels of **surface** MHC class I was studied. We also created derivatives of a non-permissive Chinese hamster ovary (CHO) cell line that expressed human class I (HLA-A2) and found that these cells did not bind fibre or take up virus. In addition, the extracellular domain of CAR was expressed in E. coli and used to generate a polyclonal anti-CAR antibody. This antibody blocked both 125I labelled fibre knob binding and virus uptake. Thus CAR, and not MHC class I, is a receptor for human **adenoviruses** in cultured tumour cells. Tissue CAR levels may therefore be an important factor in the efficiency of **adenovirus**-mediated gene therapy.

L23 ANSWER 19 OF 40 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
ACCESSION NUMBER: 1998322054 EMBASE
TITLE: Development of novel cell **surface** CD34-targeted recombinant adenoassociated virus vectors for gene therapy.
AUTHOR: Yang Q.; Mamounas M.; Yu G.; Kennedy S.; Leaker B.; Merson J.; Wong-Staal F.; Yu M.; Barber J.R.
CORPORATE SOURCE: Dr. J.R. Barber, Immusol, Inc., 3050 Science Park Road, San Diego, CA 92121, United States
SOURCE: Human Gene Therapy, (1 Sep 1998) 9/13 (1929-1937).
Refs: 25
ISSN: 1043-0342 CODEN: HGTHE3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
022 Human Genetics
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Recombinant adenoassociated virus (rAAV) type 2 vectors have been used to transduce a wide variety of cell types, including hematopoietic progenitor cells. For in vivo gene transfer, it is desirable to have an rAAV vector that specifically transduces selected target cells. As a first step toward generating an rAAV vector capable of targeting delivery in vivo, we have engineered a chimeric protein combining the AAV **capsid** protein and the variable region of a single-chain antibody against human CD34 molecules, a cell **surface** marker for hematopoietic stem/progenitor cells. Inclusion of the chimeric CD34 single-chain antibody-AAV **capsid** proteins within an rAAV virion significantly increased the preferential infectivity of rAAV for the CD34+ human myoleukemia cell line KG-1, which is normally refractory to rAAV transduction. Antibodies against the single-chain antibody and the CD34 protein blocked this transduction. This chimeric vector represents a significant improvement in the host range of rAAV and the first step toward specific gene delivery by rAAV vectors to cells of choice, in this case, hematopoietic progenitor cells, for the treatment of human disease.

L23 ANSWER 28 OF 40 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 94157452 MEDLINE
DOCUMENT NUMBER: 94157452 PubMed ID: 7509367
TITLE: Expression of a foreign epitope on the **surface** of the **adenovirus** hexon.
AUTHOR: Crompton J; Toogood C I; Wallis N; Hay R T
CORPORATE SOURCE: Division of Cell and Molecular Biology, School of Biological and Medical Sciences, University of St Andrews, Fife, U.K.
SOURCE: JOURNAL OF GENERAL VIROLOGY, (1994 Jan) 75 (Pt 1) 133-9. Journal code: 0077340. ISSN: 0022-1317.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199403
ENTRY DATE: Entered STN: 19940406
Last Updated on STN: 19970203
Entered Medline: 19940329

AB To present short protein sequences to the host immune system a foreign epitope has been expressed on the **surface** of the **adenovirus** virion as part of the hexon. As the trimeric hexon constitutes 240 out of the 252 capsomers of the virus, the foreign epitope is repeated 720 times on the virion **surface**. An eight amino acid sequence from the major **antigenic** site in the VP1 **capsid** protein of poliovirus type 3 was engineered into two regions of the **adenovirus** type 2 hexon. The two loop regions chosen to accommodate the foreign sequences are exposed on the **surface** of the virion, show sequence variation between serotypes and are the sites of interaction with neutralizing antibodies. Virus with substitutions in loop I had wild-type growth characteristics, whereas virus with substitutions in loop II grew poorly. **Adenoviruses** with poliovirus sequences in loop I were recognized and efficiently neutralized by antisera specific for the poliovirus sequence; an antiserum raised against the **adenovirus** with the poliovirus insert specifically recognized the VP1 **capsid** protein of poliovirus type 3. It is therefore feasible to alter the **surface** properties of the **adenovirus** virion and in doing so to manipulate the immune response to this virus.